--FIELD OF THE INVENTION

C2 The invention relates to a pharmaceutical preparation comprising the vWF-propeptide (pp-vWF).--

Please replace the second paragraph on page 1, with the following rewritten paragraph:

--BACKGROUND OF THE INVENTION

Von Willebrand factor (vWF) is a glycoprotein circulating in plasma as a series of multimers ranging in size from about 500 to 20,000 kD. Multimeric forms of vWF are composed of 250 kD polypeptide subunits linked together by disulfide bonds. vWF mediates the initial platelet adhesion to the sub-endothelium of the damaged vessel wall, only the larger multimers also exhibiting hemostatic activity. It is assumed that endothelial cells secret large polymeric forms of vWF and that those forms of vWF which have a low molecular weight (low molecular weight vWF) have arisen from proteolytic cleavage. The multimers having large molecular masses are stored in the Weibel-Pallade bodies of the endothelial cells and liberated upon stimulation.--

C3

Please delete the first full paragraph on page 3 (i.e., the paragraph beginning "Although pharmaceutical preparations containing . . .") and the second full paragraph on page 3 (i.e., the paragraph beginning "From Blann et al. . . .").

Please replace the third full paragraph on page 3, with the following rewritten paragraph:

--SUMMARY OF THE INVENTION

C4 It is the object of the present invention to provide a vWF pharmaceutic with improved properties. The preparation should enhance the intrinsic blood coagulation activity in individuals and reduce the arterial thrombotic risk of vWF therapy.--

Please replace the final paragraph beginning on page 3, with the following rewritten paragraph:

--The object is solved by the present invention by providing a pharmaceutical preparation for treating blood coagulation disorders comprising an effective amount of vWF propeptide. It was found out that pp-vWF plays an essential role in blood coagulation. It promotes the intrinsic blood coagulation and thereby acts on secondary hemostasis. At the same time it inhibits the platelet adhesion and controls the primary hemostatic activity of mature vWF by binding to collagen. Based on these findings, a vWF preparation can be improved providing additional pro-vWF or pp-vWF as a separate effective protein in the vWF preparation. pp-vWF controls the primary hemostatic activity of the mature vWF and thus reduces the potential thrombotic risk of vWF, for example inducing arterial thrombosis as indicated by the prior art.--

Please insert the following paragraphs on page 4 before the final paragraph beginning "The preparation of the pp-vWF . . . ":

--BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 shows the effect of pro-vWF on the thrombin generation in plasma in the presence of platelets.

Fig. 2 shows the dose dependence effect of pro-vWF on the thrombin generation in plasma in the presence of platelets.

Figs. 3a and 3b show the comparison of the in vivo effect of pro-vWF and plasma derived vWF in a dog.

DETAILED DESCRIPTION--

Please replace the final paragraph beginning on page 9, with the following rewritten paragraph:

--Yet another aspect of the present invention is the use of pp-vWF and/or pro-vWF containing the pp-vWF for the preparation of a pharmaceutical composition for treating a patient at a risk of blood coagulation disorders, such as vWD, hemophilia (e.g. phenotypic hemophilia, hemophilia A and factor VIII inhibitors).--

C7

Please replace the first full paragraph on page 10, with the following rewritten paragraph:

--The effective dosage of the preparation when applied will vary depending on the respective syndrome and preferably should be chosen after determination of the blood levels of the critical blood factors or risk for thrombosis in the patient. The optimum dosage also depends on whether or not the parenteral, preferably intravenous, subcutaneous or intramuscular administration is to be effected in bolus form or as a depot. By using a suitable carrier material such as liposomes a peroral administration is feasible. It also depends on whether it is to be applied systemically and/or locally at the site of the blood coagulation disorder.--

C8

Please delete the second, third and fourth full paragraphs on page 11 (i.e., the paragraphs describing Figures 1, 2 and 3a and 3b).

Please replace the final paragraph on page 13 with the following rewritten paragraph:

--Thrombin potential increased in parallel with the increase of propeptide after the treatment with a recombinant pro-vWF preparation. ELISA results showed, that a few percent of pro-vWF remained in the circulation after 15 minutes, and it could no longer be detected (data not shown), but a significant increase in the propeptide and vWF was observed. In contrast, no propeptide and also no substantial thrombin potential was

C9